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## OBSERVATIONS ON ANTIBODY FORMATION IN TYPHOID.\*

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It has been shown repeatedly that there is a marked increase of antibodies in the blood following inoculation against typhoid fever. In a previous article<sup>1</sup> I have described the course of the curve of agglutination for a period of two years following such inoculation. At the end of that time the agglutinins have decreased to practically the normal amount which was present before the injections of killed bacilli were made. If we assume that resistance to disease runs parallel with the amount of antibodies present in the serum we would conclude that the artificially induced resistance to typhoid had practically disappeared after two years. However such an assumption is not justifiable. The rapidity with which antibodies are produced is as important a factor in the production of resistance as is the relative amount of antibodies present. Cole<sup>2</sup> observed that a guinea-pig which had been previously injected with typhoid bacilli on being reinjected responded promptly by a rapid and abundant formation of antibodies, while a normal guinea-pig treated similarly responded slowly and gave a comparatively low curve. Other observers have recorded similar results. The following experiment was made in order to observe the behavior of the agglutinin curve in human subjects.

Persons who had previously received antityphoid inoculation or had had typhoid fever were given a single injection of killed typhoid bacilli. Other persons of about the same age who had received no previous inoculation and had not had typhoid fever were injected similarly. The blood was tested daily for agglutinins by determining at what dilution the serum would produce noticeable agglutination in a suspension of young, motile, typhoid bacilli. This was determined by microscopic examination after 45 minutes at 37° C.

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<sup>1</sup> *Jour. Amer. Med. Assn.*, 1913, 60, p. 1764.

<sup>2</sup> *Ztschr. f. Hyg. u. Infektionskrankh.*, 1904, 66, p. 367.

The results are represented graphically in the following charts which trace the curve of agglutination for 15 days following the injection. The vertical lines mark days while the horizontal lines indicate the dilution of the sera.

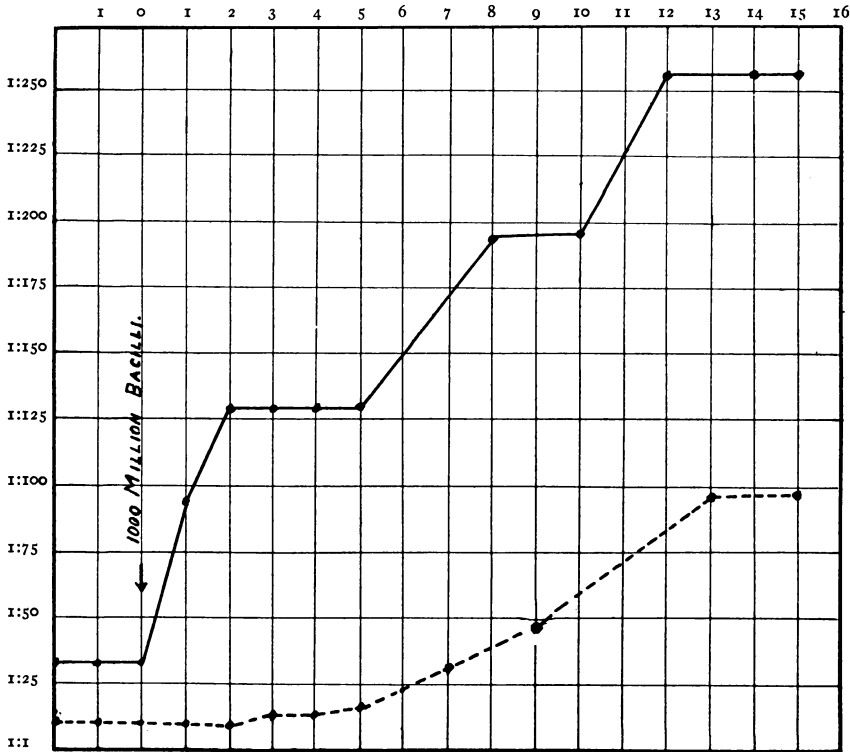


CHART 1.—The solid line represents the curve of a person who had received typhoid inoculation two and one-half years previously. The line of dashes represents the control. Both received an injection of 1,000 million killed bacilli on the day indicated.

As shown by these curves there is a distinct difference in the rapidity with which human beings who have previously been immunized form antibodies as compared with those who have not. It would seem as if the previously immunized person remains more sensitive to the antigenic influence of typhoid bacilli and responds more quickly by the production of antibodies when the bacilli are introduced into the system. Such a result is in keeping with our knowledge of the phenomena of allergy. That this condition would



CHART 2.—The solid line represents the curve of a person who had received protective inoculation one and one-half years previously. The line of dashes represents the control. 500 million killed bacilli were injected in each on the day indicated.

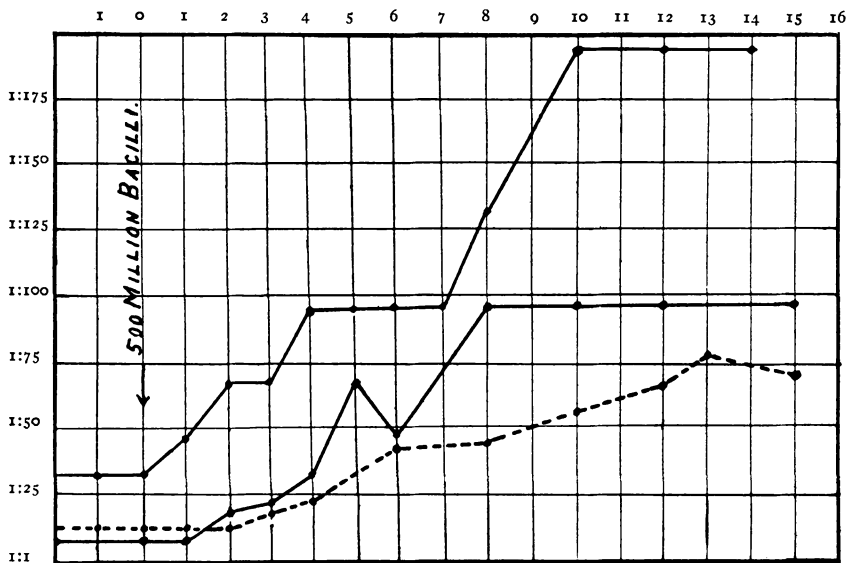


CHART 3.—The solid lines represent the curves of two persons who had had typhoid fever 12 years previously. The line of dashes represents the average curve of two controls who had no typhoid history. 500 million killed bacilli were injected on the day indicated.

contribute to the resistance against typhoid and the readiness with which the body would overcome the bacilli is easily understood. Chart 3 would indicate that the same condition exists after an attack of typhoid fever, but that the degree of excitability is slight after a period of 12 years.

Rolly and Meltzer<sup>1</sup> found that typhoid agglutinins and bacteriolysins are produced more abundantly in rabbits under conditions of experimental hyperthermia. On the other hand, Graziani<sup>2</sup>

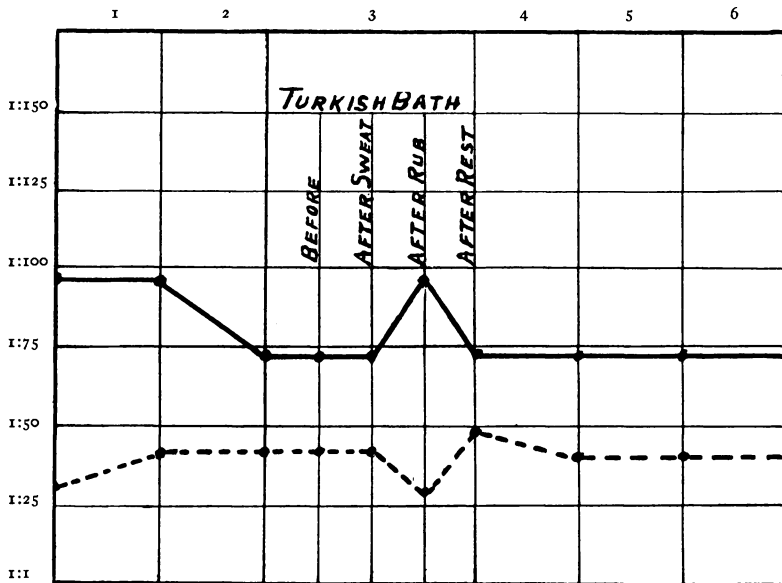


CHART 4.—The two curves here shown represent the agglutinins in the sera of two persons before, during, and after the Turkish bath.

found that when rabbits are injected with filtrates of typhoid cultures and are subsequently kept at different temperatures, those kept at a temperature slightly above freezing developed more agglutinins than those kept at higher temperatures.

Von Leube<sup>3</sup> found that patients recovering from typhoid fever showed a material increase in the agglutinin content of the blood after hot baths, 40° C. for 30 minutes.

<sup>1</sup> *Deutsch. Arch. f. kl. Med.*, 1909, 94, p. 385.

<sup>2</sup> *Centralbl. f. Bakteriolog.*, I, Orig., 1907, 42, p. 633.

<sup>3</sup> *Verhandl. d. deutsch. Kongresses f. inn. Med.*, 1910, 27, p. 218.

These observations suggested the question whether a transient elevation of temperature such as may be attained in a Turkish bath, would cause any perceptible change in the antibody content of the sera of persons immunized to typhoid bacilli. Accordingly persons who had received antityphoid inoculation several weeks previously were selected for experiment. They were taken through the routine of the Turkish bath which consisted of 30 minutes in the dry room at a temperature of 180° F., 20 minutes in the steam room at a temperature of 130° F., followed by massage, rub, shower bath, and an hour's rest. Samples of serum taken before, during, and after the Turkish bath were tested for agglutinins as in the experiments previously described. Chart 4 represents the curves of two persons so treated. The only variation observed occurred in the samples taken after the massage and rub, and these variations were of opposite character in the two cases. This variation was transient and so slight in degree that it might be accounted for as due to the greater concentration of the serum following profuse perspiration, or to experimental error.

#### SUMMARY.

We should conclude then that the protective effect of anti-typhoid inoculation lasts for a longer period than two years, and that this effect is due not so much to the persistence of antibodies in the blood as to the promptness with which new antibodies are formed in the presence of typhoid proteins.

Turkish baths probably do not materially affect the concentration of agglutinins in the sera of persons inoculated with typhoid bacilli.